REMARKS

Reconsideration of this application is respectfully requested. Claims 18-32 and 42-51 are withdrawn from consideration. Claims 3 and 17 have been cancelled without prejudice or disclaimer. Claims 1 and 9 have been amended without prejudice or disclaimer. By this Amendment, no new matter has been added to the application. Upon entry of this Amendment, claims 1, 2, 4-16 and 33-40 are pending.

Amendments to the Claims

Claim 1 has been amended to incorporate the limitation of claim 3. Support for this amendment can be found in original claim 3. No new matter has been added by this amendment. Claim 9 has been amended to incorporate the limitation of claim 17. Support for this amendment can be found in original claim 17. No new matter has been added by this amendment.

Rejections under 35 U.S.C. § 102(e) or alternatively 35 U.S.C. § 103(a)

Claims 1, 2, 4-14, 16, 33-36 and 38-39 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by, or under 35 U.S.C. § 103(a) as alternatively obvious over, Matzinger U.S. Patent No. 6,376,611 ("Matzinger"). The Examiner states that while Matzinger does indeed teach "hot melt inks," that the Matzinger inks comprise the same compounds and are applied to the same substrates as the present application, and that they are dried as in the present application. In this Action, the Examiner also states that the inked and dried substrate of Matzinger, and the process of making it, are equivalent to the lithographic printing form, and process of making the lithographic printing form, of the present invention.

Amended claim 1 calls for a baked ink, and amended claim 9 calls for a process that bakes the ink into the substrate. The specification describes the ink and exemplary methods of the present invention:

> After being placed on a substrate such as a metal plate, preferably made of aluminum and being dried and baked at temperatures above 120°C,

> preferably between 170°C and 220°C, and optimally between 190°C and 210°C, the resulting mixture creates an interlinking cross-binded network. This network binds strongly to the surface of the substrate, and the resulting product is the lithographic print form. During the heating the ink is baked into the surface of the substrate. See page 11, lines 5-7 of the specification, WO 2004/037934.

Matzinger fails to disclose either a baked ink or a method of preparing a lithographic printing form by baking the ink into the substrate. Furthermore, Matzinger fails to teach or suggest an ink mixture that creates an interlinking cross-bound network, which is baked into the surface of the substrate. Accordingly, Matzinger does not anticipate, nor is alternatively obvious over the pending claims.

Claims 2, 4-8, 10-14, 16, 33-36 and 38-39 depend directly or indirectly from amended claims 1 or 9, and thus none of these claims are anticipated by Mohan. Withdrawal of the rejection of claims 1, 2, 4-14, 16, 33-36 and 38-39 for anticipation, or in the alternative obviousness, over Matzinger is respectfully requested.

Rejections under 35 U.S.C. § 102(e)

Claims 1-6, 8-13, 16, 33 and 36 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Aurenty et al. U.S. Patent No. 6,472,054 ("Aurentry"). The Examiner contends that Aurentry discloses that a printing plate is prepared by ink jetting to a substrate, where the ink comprises an acidic polymeric compound and the acid groups of the polymeric compound are neutralized with ammonia or an amine base. The Examiner further contends that neutralization of the acidic groups of a polymer with ammonia "is equivalent to the formation of amide groups of the instant application."

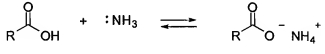
Amended claim 1 of the present invention calls for a baked ink, and amended claim 9 calls for a process wherein the ink is baked into the substrate. Aurentry discloses a "printing plate that is ready-to-use on a press without having to develop it" (See Aurentry Abstract). The

working examples show that the resulting plates are used without processing or curing (See column 8, lines 14-16, lines 60-63, and column 9, lines 21-23 of Aurentry). Aurentry fails to teach a baked ink or an ink mixture that creates an interlinking cross-bound network, which is baked into the surface of the substrate.

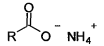
The Examiner further states that claim 3 of the present invention is anticipated by Aurentry because claim 3 is a product-by-process claim and that limitation "wherein the ink is baked ink" does not give any patentable weight to the claimed product, and that the dried and hardened ink of Aurentry is identical to the dried and hardened ink obtained by baking.

The Examiner's rejection of claim 3, and claims 1, 2, 4-6, 8-13, 16, 33 and 36, is based on the incorrect assumption that neutralization of an acid group is equivalent to the formation of an amide. However, the neutralization of an acid with an amine base forms an ammonium salt with the acid and not an amide as the Examiner contends. Therefore, the ink of Aurentry is not equivalent to the ink called for by the present claims.

The textbook, Organic Chemistry, Fourth Edition by John McMurry of Cornell University, ("McMurry") explains, "[a]mides are difficult to prepare by direct reaction of carboxylic acids with amines because amines are bases that convert acidic carboxyl groups into their carboxylate anions" (See page 815 of McMurry). McMurry includes the following scheme:



An ammonium carboxylate salt is structurally different from an amide:



ammonium carboxylate salt

amide

McMurry goes on to say, "[s]ince the carboxylate anion has a negative charge, it is no longer electrophilic and no longer likely to be attacked by nucleophiles except at high temperature" (See page 815 of McMurry, emphasis added).

Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, Fourth Edition, , by Jerry March of Adelphi University confirms this fact, "[w]hen carboxylic acids are treated with ammonia or amines, salts are obtained" (See page 419, fourth paragraph of March). March goes on to describe that amides can be obtained at room temperature, but require the addition of a coupling agent (See, for example, page 419, last paragraph to page 420, first paragraph).

Aurentry fails to disclose either elevated temperatures or a coupling agent, both of which would be required in order to form an amide. Furthermore, the disclosure by Aurentry appears to describe the formation of the carboxylate salt:

> The acidic polymeric compound is at least partially neutralized with base, preferably ammonia, to create the conjugate base groups that can react with the substrate and form the ink-receiving layer. See column 5, lines 47-50.

The term "neutralized" is indicative of an acid-base reaction in which a "salt" is formed, in this case a carboxylate salt. The Aurentry disclosure does not support the formation of an amide, which would require additional energy in the form of heat, or the addition of a coupling agent, neither of which are disclosed.

Therefore Aurentry fails to disclose the ink of the present claims. Withdrawal of the rejection of claims 1-6, 8-13, 16, 33 and 36 for anticipation by Aurentry is respectfully requested.

Claims 1-6, 9-13, 15, 17, 33-40 are rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Cottrell *et al.* WO 00/29493 ("Cottrell"). The Examiner states that Cottrell discloses a process of preparing a patterned acrylic film on a substrate by applying an ink mixture comprising one or more crosslinked acrylic polymers containing a carboxylic acid group, such as acrylic acid, methacrylic acid, fumaric acid. The Examiner further states that Cottrell discloses that the acid groups may be fully or partially neutralized with bases, such as

ammonia or amines (triethylamine, triethanolamine) and that neutralization of an acidic group with ammonia or an amine "is equivalent to the formation of amide groups of the instant application."

For the reasons set forth above in response to the Examiner's rejection of claims over Aurentry, the neutralization of an acid with an amine base does not form an amide. As Cottrell states, "[t]he acid groups may be subsequently fully or partially neutralized with a base containing a cationic charge to give a salt" (See page 8, lines 20-21 of Cottrell). Therefore, the ink of Cottrell contains carboxylate salts after neutralization, and not amides. Therefore, the Cottrell ink is not equivalent to the ink called for by the present claims.

In addition, Cottrell discloses that the precursors for the polymers of the ink are preferably hydrophilic (See page 6, line 20 of Cottrell), and that polymers comprising water dispersing groups are used (page 6, lines 16-20 and page 8, line 10 to page 9, line 14). These dispersing groups render the polymers dispersable or soluble in water, implying that they are hydrophilic. In contrast, the ink of the pending claims is hydrophobic, and presents a hydrophobic surface representing the transferred image, while the remainder of the plate is hydrophilic (See page 9, lines 14-23 of the specification, WO 2004/037934).

Thus for at least these reasons, the ink of Cottrell is not equivalent to the ink called for in the present claims. Withdrawal of the rejection of claims 1-6, 9-13, 15, 17, 33-40 for anticipation by Cottrell is respectfully requested.

This application is believed to be in condition for allowance, which is earnestly solicited. If the Examiner believes there are remaining issues that could be resolved through an interview or an Examiner's amendment, the Examiner is cordially invited to contact the undersigned agent.

Dated: August 4, 2008

Respectfully submitted,

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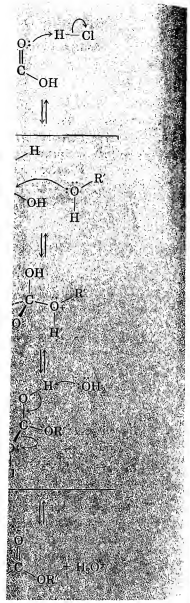

he reaction is an acid-catalyzed,

port of the mechanism shown
periments. When ^{18}O-labeled
l benzoate produced is found
labeled. Thus, it is the CO–OH
ring the reaction rather than
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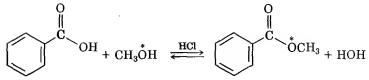


PROBLEM

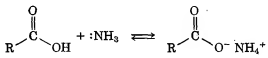
21.5 How would you prepare the following esters?
(a) Butyl acetate (b) Methyl butanoate

PROBLEM

21.6 If 5-hydroxypentanoic acid is treated with acid catalyst, an intramolecular esterification reaction occurs. What is the structure of the product? (*Intramolecular* means within the same molecule.)

Conversion of Carboxylic Acids into Amides

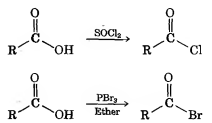
Amides are difficult to prepare by direct reaction of carboxylic acids with amines because amines are bases that convert acidic carboxyl groups into their carboxylate anions. Since the carboxylate anion has a negative charge, it is no longer electrophilic and no longer likely to be attacked by nucleophiles except at a high temperature. We'll see a better method for making amides from acids in Section 27.11 in connection with the synthesis of proteins from amino acids.



21.5 Chemistry of Acid Halides

Preparation of Acid Halides

Acid chlorides are prepared from carboxylic acids by reaction with thionyl chloride ($SOCl_2$), as we saw in the previous section. Reaction of a carboxylic acid with phosphorus tribromide (PBr_3) yields the acid bromide.



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:d amides, primary amines give
stituted amides. Arylamines can
d to combine with the liberated
0-20.
to give, respectively, hydrazides
hese compounds are often made
ic and aromatic primary amines
ocyanates RNCO.[846] This is one
inates.[847] Thiophosgene,[847a] sim-

$\xrightarrow{Cl}$ O=C=N—R

'or phosgene in this reaction is
roformates ROCOCl are treated
d.[849] An example of this reaction
oup of amino acids and peptides:

—O—C—NHR
‖
O

, and is often abbreviated Cbz or
ycarbonyl group Me_3COCO, ab-
Cl is unstable, so the anhydride
mino groups in general are often
halides with lithium nitride gives

)$_3$N

51

, 415, 488, 490, 613; **IV,** 339, 411,
307; **67,** 187; **68,** 83. See also OS

$-NH_2$ + R'COOH

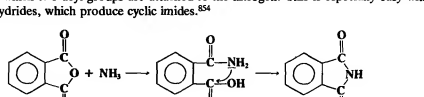
55, pp. 515-600.
63, *13*, 1053.
othiocyanates, see, respectively, the articles
03-1221, in Patai *The Chemistry of Cyanates*

0. For a review of the industrial preparation
09-230.
100.

1985, *15*, 1025.

See also Song; Jencks *J. Am. Chem. Soc.*

This reaction, similar in scope and mechanism[852] to **0-52,** can be carried out with ammonia or primary or secondary amines.[853] However, ammonia and primary amines can also give imides, in which two acyl groups are attached to the nitrogen. This is especially easy with cyclic anhydrides, which produce cyclic imides.[854]



The second step in this case, which is much slower than the first, is the attack of the amide nitrogen on the carboxylic carbon. Unsubstituted and N-substituted amides have been used instead of ammonia. Since the other product of this reaction is RCOOH, this is a way of "hydrolyzing" such amides in the absence of water.[855]

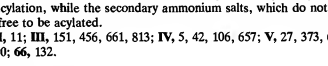
Even though formic anhydride is not a stable compound (see p. 542), amines can be formylated with the mixed anhydride of acetic and formic acids HCOOCOMe[856] or with a mixture of formic acid and acetic anhydride. Acetamides are not formed with these reagents. Secondary amines can be acylated in the presence of a primary amine by conversion to their salts and addition of 18-crown-6.[857] The crown ether complexes the primary ammonium salt, preventing its acylation, while the secondary ammonium salts, which do not fit easily into the cavity, are free to be acylated.

OS **I,** 457; **II,** 11; **III,** 151, 456, 661, 813; **IV,** 5, 42, 106, 657; **V,** 27, 373, 650, 944, 973; **VI,** 1; **VII,** 4, 70; **66,** 132.

0-54 Acylation of Amines by Carboxylic Acids
Amino-de-hydroxylation

$$RCOOH + NH_3 \longrightarrow RCOO^- NH_4^+ \xrightleftharpoons{\text{pyrolysis}} RCONH_2$$

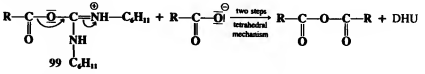
When carboxylic acids are treated with ammonia or amines, salts are obtained. The salts of ammonia or primary or secondary amines can be pyrolyzed to give amides,[858] but the method is less convenient than **0-52, 0-53,** and **0-55** and is seldom of preparative value.[859] Lactams are produced fairly easily from γ- or δ-amino acids,[860] e.g.,



Although treatment of carboxylic acids with amines does not directly give amides, the reaction can be made to proceed in good yield at room temperature or slightly above by

[852]For a discussion of the mechanism, see Kluger; Hunt *J. Am. Chem. Soc.* **1989,** *111*, 3325.
[853]For a review, see Beckwith, in Zabicky, Ref. 555, pp. 86-96.
[854]For reviews of imides, see Wheeler; Rosado, in Zabicky, Ref. 555, pp. 335-381; Hargreaves; Pritchard; Dave *Chem. Rev.* **1970,** *70*, 439-469 (cyclic imides).
[855]Eaton; Rounds; Urbanowicz; Gribble *Tetrahedron Lett.* **1988,** *29*, 6553.
[856]For the formylation of amines with the mixed anhydride of formic and trimethylacetic acid, see Vlietstra; Zwikker; Nolte; Drenth *Recl. Trav. Chim. Pays-Bas* **1983,** *101*, 460.
[857]Barrett; Lana *J. Chem. Soc., Chem. Commun.* **1978,** 471.
[858]For example, see Mitchell; Reid *J. Am. Chem. Soc.* **1931,** *53*, 1879.
[859]For a review of amide formation from carboxylic acids, see Beckwith, in Zabicky, Ref. 555, pp. 105-109.
[860]See, for example, Bladé-Font *Tetrahedron Lett.* **1980,** *21*, 2443.

the use of coupling agents,[861] the most important of which is dicyclohexylcarbodiimide. This is very convenient and is used[862] a great deal in peptide synthesis.[863] The mechanism is probably the same as in **0-22** up to the formation of **99**. This intermediate is then attacked by another molecule of $RCOO^-$ to give the anhydride $(RCO)_2O$, which is the actual species that reacts with the amine:



The anhydride has been isolated from the reaction mixture and then used to acylate an amine.[864] Other promoting agents[865] are N,N′-carbonyldiimidazole (**100**, p. 396),[664] which behaves as in reaction **0-22**, $POCl_3$,[866] $TiCl_4$,[867] sulfuryl chloride fluoride SO_2ClF,[868] benzotriazol-1-yl diethyl phosphate,[869] $Ti(OBu)_4$,[870] molecular sieves,[871] N,N,N′,N′-tetramethyl(succinimido)uronium tetrafluoroborate,[872] CBMIT[656] (p. 396), Lawesson's reagent (p. 893),[873] chlorosulfonyl isocyanate,[660] P_2I_4,[874] pyridinium salts–Bu_3N,[875] and a mixture of Bu_3P and PhCNO.[876] Certain dicarboxylic acids form amides simply on treatment with primary aromatic amines. In these cases the cyclic anhydride is an intermediate and is the species actually attacked by the amine.[877] Carboxylic acids can also be converted to amides by heating with amides of carboxylic acids (exchange),[878] sulfonic acids, or phosphoric acids, e.g.,[879]

$$\mathbf{RCOOH + Ph_2PONH_2 \longrightarrow RCONH_2 + Ph_2POOH}$$

or by treatment with trisalkylaminoboranes $[B(NHR')_3]$, with trisdialkylaminoboranes $[B(NR'_2)_3]$,[880]

$$\mathbf{RCOOH + B(NR'_2)_3 \longrightarrow RCONR'_2}$$

or with bis(diorganoamino)magnesium reagents $(R_2N)_2Mg$.[881]

[861]For a review of peptide synthesis with dicyclohexylcarbodiimide and other coupling agents, see Klausner; Bodansky *Synthesis* **1972**, 453-463.

[862]It was first used this way by Sheehan; Hess *J. Am. Chem. Soc.* **1955**, *77*, 1067.

[863]For a treatise on peptide synthesis, see Gross; Meienhofer *The Peptides*, 3 vols.; Academic Press: New York, 1979-1981. For a monograph, see Bodanszky; Bodanszky *The Practice of Peptide Synthesis*; Springer: New York, 1984.

[864]Schüssler; Zahn *Chem. Ber.* **1962**, *95*, 1076; Rebek; Feitler *J. Am. Chem. Soc.* **1974**, *96*, 1606. There is evidence that some of the **99** is converted to products by another mechanism. See Rebek; Feitler *J. Am. Chem. Soc.* **1973**, *95*, 4052.

[865]For a list of reagents, with references, see Ref. 508, pp. 972-976.

[866]Klosa *J. Prakt. Chem.* **1963**, [4] *19*, 45.

[867]Wilson; Weingarten *Can. J. Chem.* **1970**, *48*, 983.

[868]Olah; Narang; Garcia-Luna *Synthesis* **1980**, 661.

[869]Kim; Chang; Ko *Tetrahedron Lett.* **1985**, *26*, 1341.

[870]Shteinberg; Kondratov; Shein *J. Org. Chem. USSR* **1988**, *24*, 1774.

[871]Cossy; Pale-Grosdemange *Tetrahedron Lett.* **1989**, *30*, 2771.

[872]Bannwarth; Knorr *Tetrahedron Lett.* **1991**, *32*, 1157.

[873]Thorsen; Andersen; Pedersen; Yde; Lawesson *Tetrahedron* **1985**, *41*, 5633.

[874]Suzuki; Tsuji; Hiroi; Sato; Osuka *Chem. Lett.* **1983**, 449.

[875]Bald; Saigo; Mukaiyama *Chem. Lett.* **1975**, 1163. See also Mukaiyama; Aikawa; Kobayashi *Chem. Lett.* **1976**, 57.

[876]Grieco; Clark; Withers *J. Org. Chem.* **1979**, *44*, 2945.

[877]Higuchi; Miki; Shah; Herd *J. Am. Chem. Soc.* **1963**, *85*, 3655.

[878]For example, see Schindbauer *Monatsh. Chem.* **1968**, *99*, 1799.

[879]Zhmurova; Voitsekhovskaya; Kirsanov *J. Gen. Chem. USSR* **1959**, *29*, 2052. See also Kopecký; Šmejkal *Chem. Ind.* (*London*) **1966**, 1529; Liu; Chan; Lee *Synth. Commun.* **1979**, *9*, 31.

[880]Pelter; Levitt; Nelson *Tetrahedron* **1970**, *26*, 1539; Pelter; Levitt *Tetrahedron Lett.* **1970**, *26*, 1545, 1899.

[881]Sanchez; Vest; Despres *Synth. Commun.* **1989**, *19*, 2909.

An important technique, discovered by R. B. Merrifield in 1963[882] and since used for the synthesis of many peptides,[883] is called *solid phase synthesis* or *polymer-supported synthesis*.[884] The reactions used are the same as in ordinary synthesis, but one of the reactants is anchored onto a solid polymer. For example, if it is desired to couple two amino acids (to form a dipeptide), the polymer selected might be polystyrene with CH_2Cl side chains (Fig. 10.2, **103**). One of the amino acids, protected by a *t*-butoxycarbonyl group (Boc), would then be coupled to the side chains (step A). It is not necessary that all the side chains be converted, but a random selection will be. The Boc group is then removed by hydrolysis with trifluoroacetic acid in CH_2Cl_2 (step B) and the second amino acid is coupled to the first, using DCC or some other coupling agent (step C). The second Boc group is removed (step D), resulting in a dipeptide that is still anchored to the polymer. If this dipeptide is the desired product, it can be cleaved from the polymer by various methods,[885] one of which is treatment with HF (step E). If a longer peptide is wanted, additional amino acids can be added by repeating steps C and D.

The basic advantage of the polymer support techniques is that the polymer (including all chains attached to it) is easily separated from all other reagents, because it is insoluble in the solvents used. Excess reagents, other reaction products (such as DHU), side products, and the solvents themselves are quickly washed away. Purification of the polymeric species (such as **104, 105,** and **106**) is rapid and complete. The process can even be automated,[886] to the extent that six or more amino acids can be added to a peptide chain in one day. Commercial automated peptide synthesizers are now available.[887]

Although the solid phase technique was first developed for the synthesis of peptide chains and has seen considerable use for this purpose, it has also been used to synthesize chains of polysaccharides and polynucleotides; in the latter case, solid phase synthesis has almost completely replaced synthesis in solution.[888] The technique has been applied less often to reactions in which only two molecules are brought together (nonrepetitive syntheses), but many examples have been reported.[889]

OS **I,** 3, 82, 111, 172, 327; **II,** 65, 562; **III,** 95, 328, 475, 590, 646, 656, 768; **IV,** 6, 62, 513; **V,** 670, 1070; **69,** 55. Also see OS **III,** 360; **VI,** 263; **67,** 69.

0-55 Acylation of Amines by Carboxylic Esters
Amino-de-alkoxylation

$$\mathbf{RCOOR' + NH_3 \longrightarrow RCONH_2 + R'OH}$$

[882]Merrifield *J. Am. Chem. Soc.* **1963,** *85,* 2149.

[883]For a monograph on solid state peptide synthesis, see Birr *Aspects of the Merrifield Peptide Synthesis*; Springer: New York, 1978. For reviews, see Bayer *Angew. Chem. Int. Ed. Engl.* **1991,** *30,* 113-129 [*Angew. Chem.* **103**, 117-133]; Kaiser *Acc. Chem. Res.* **1989,** *22,* 47-54; Jacquier *Bull. Soc. Chim. Fr.* **1989,** 220-236; Barany; Kneib-Cordonier; Mullen *Int. J. Pept. Protein Res.* **1987,** *30,* 705-739; Andreev; Samoilova; Davidovich; Rogozhin *Russ. Chem. Rev.* **1987,** *56,* 366-381; in vol. 2 of Ref. 863, the articles by Barany; Merrifield, pp. 1-184, Fridkin, pp. 333-363; Erickson; Merrifield, in Neurath; Hill; Boeder *The Proteins*, 3rd ed., vol. 2; Academic Press: New York, 1976, pp. 255-527. For R. B. Merrifield's Nobel Prize lecture, see Merrifield *Angew. Chem. Int. Ed. Engl.* **1985,** *24,* 799-810 [*Angew. Chem.* **97**, 801-812], *Chem. Scr.* **1985,** *25,* 121-131.

[884]For monographs on solid phase synthesis in general, see Laszlo *Preparative Organic Chemistry Using Supported Reagents*; Academic Press: New York, 1987; Mathur; Narang; Williams *Polymers as Aids in Organic Chemistry*; Academic Press: New York 1980; Hodge; Sherrington *Polymer-supported Reactions in Organic Synthesis*; Wiley: New York, 1980. For reviews, see Sheppard, *Chem. Br.* **1983,** 402-414; Pillai; Mutter *Top. Curr. Chem.* **1982,** *106,* 119-175; Akelah; Sherrington *Chem. Rev.* **1981,** *81,* 557-587; Akelah *Synthesis* **1981,** 413-438; Rebek *Tetrahedron* **1979,** *35,* 723-731; McKillop; Young *Synthesis* **1979,** 401-422, 481-500; Neckers, *CHEMTECH* **1978** (Feb.), 108-116; Crowley; Rapoport *Acc. Chem. Res.* **1976,** *9,* 135-144; Patchornik; Kraus *Pure Appl. Chem.* **1975,** *43,* 503-526.

[885]For some of these methods, see Whitney; Tam; Merrifield *Tetrahedron* **1984,** *40,* 4237.

[886]This was first reported by Merrifield; Stewart; Jernberg *Anal. Chem.* **1966,** *38,* 1905.

[887]For a discussion of automated organic synthesis, see Frisbee; Nantz; Kramer; Fuchs *J. Am. Chem. Soc.* **1984,** *106,* 7143. For an improved method, see Schnorrenberg; Gerhardt *Tetrahedron* **1989,** *45,* 7759.

[888]For a review, see Bannwarth *Chimia* **1987,** *41,* 302-317.

[889]For reviews, see Fréchet *Tetrahedron* **1981,** *37,* 663-683; Fréchet, in Hodge; Sherrington, Ref. 884, pp. 293-342, Leznoff, *Acc. Chem. Res.* **1978,** *11,* 327-333, *Chem. Soc. Rev.* **1974,** *3,* 64-85.